REMARKS

The applicant elects Group I with traverse. The Examiner has not shown that the claims are directed to independent and distinct inventions and for this reason, it is requested that the Restriction Requirement be withdrawn.

An Information Disclosure Statement is being submitted with this Amendment to list the patents that were cited in the specification as background prior art for pharmaceutical formulations. The patents which describe the active ingredients have not been cited on the Information Disclosure Statement because it is understood that they describe methods of making the various active ingredients and not controlled release formulations.

Claims 12-13, 44-45 and 70 were objected to as being in improper form. Claim 70 has been amended to be a proper multiple dependent claim by placing the claim in alternative dependent form. Claims 12 and 13 are not substantial duplicates of claims 4 and 5 because claim 4 describes micro matrix particles comprising one or more hydrophobic release controlling agents whereas claim 12 depicts **coating** of micro matrix particles comprising one or more hydrophobic release controlling agents. Claim 5 and claim 13 are dependent on 4 and 12 respectively which set forth a list of hydrophobic release controlling agents.

Claims 44 and 45 are not substantial duplicates of claims 36 and 37 because claim 36 describes micro matrix particles comprising one or more hydrophobic release controlling agents whereas claim 44 depicts coating of micro matrix particles comprising one or more hydrophobic release controlling agents. Claim 37 and claim

45 are dependent on 36 and 44 respectively describing list of hydrophobic release controlling agents. For these reasons, it is requested that these objections be withdrawn.

Claim 1 and 33 has been amended to point out the elements of the dual release system without using the expression "dual release". This amendment clarifies the text of the original claim and does not introduce new matter. Hence, it is requested that the objection to claims 1 and 33, along with dependent claims 2-29 and 34-72, be withdrawn.

Claim 3 and 35 has been canceled and is not longer at issue.

In each of claim 5, 13, 37 and 45, the expression "such as" been deleted and where appropriate, Markush language has been introduced into the claims.

Claims 6 and 38 have been amended to delete the term "preferably".

Claims 7 and 39 have been amended to delete the term "preferred". Claims 7 and 39 have been reviewed and it is believed that they include the generic terminology for the Eudragit products and also ® is introduced to respect the specific trademark.A minor amendment has been made to revise "ammonio" to read --ammonium--Claims 9-11,17-18, 41-43, 49-50 and 64-65 have been amended to delete the phrases "preferably", "more preferably" and " most preferably".

Claims 63-67 have been amended to be directly or indirectly dependent on claim 60. For these reasons, it is requested that this ground of rejection be withdrawn.

Claims 1, 21-22, 24 and 25 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis et al.(Paradissis).

Claims 1 and 4-5 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis et al.(Paradissis).

Claims 1, 8-11 and 16-18 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis et al.(Paradissis).

Claims 1, 19-20 and 23 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis et al.(Paradissis).

Claims 1 and 28-29 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis et al.(Paradissis).

Claims 1 and 14-15 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis et al.(Paradissis).

Claims 1, 26 and 32 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis et al.(Paradissis).

Claims 1 and 27 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis et al.(Paradissis).

Reconsideration is requested.

All of the claims that have been rejected under Glassman in view of Paradissis are directly or indirectly dependent on claim 1. Since the principal argument for patentability is directed to the non-obviousness of claim 1, the rejections of the separately grouped claims is being collectively addressed.

Amended claim 1 of the present application, points out that the claimed dosage form is a combination of a highly soluble active ingredient and a low dose active ingredient.
Nothing in the cited references suggests the claimed dosage form with the particularly identified ingredients. Claim 4 points out that the micro-matrix release particles comprise a hydrophobic agent as a release rate controlling agent. None of the cited references disclose a micro matrix particle formulation having a hydrophobic release rate controlling agent and a coating on micro-matrix particles. The cited claims which are directly or indirectly dependent on claim 1 point out known drugs and excipients that are used according to claim. None of the specific excipients and active drugs are used in the cited references in such a manner that a combination of a low dose drug and a highly soluble drug are placed together in a combination having controlled release properties is made obvious.

The Glassman patent discloses, a super fast starting, sustained release tablet that has two layers that are fused together by compression with talc or talc and starch. To increase the rate of dissolution, one layer contains a mixture of potassium bicarbonate or sodium bicarbonate and an acid. These materials in the presence of water generate carbon dioxide that helps to break apart the tablet. The Glassman dosage form has only one drug which is formulated for a burst or immediate release and for a subsequent extended release. Paradissis discloses an extended release pharmaceutical dosage form which is adapted to release the active drug over a 12 hour period at a zero order release rate. The release is controlled by diffusion from a core which contains a mixture of immediate release particles that have a core of a drug, inert spherical particles and a binder that is coated with talc. The talc is required to

prevent the drug layer from interfering with film formation on the particles and to prevent drug migration during storage.

There is no teaching or suggestion in either Glassman or Paradissis that would direct one skilled in the art to selectively combine the teachings of Glassman and Paradissis for the purpose of making a combination dosage form having a low dose drug and a drug which has a high solubility.

It has found by the present inventor that when the difference between the dosage strengths of two components of a dosage form is very high and particularly when the drugs are highly soluble, it is very difficult to provide a sustained release drug formulation. Nothing in the cited references addresses this problem.

For these reasons, it is requested that these grounds of rejection be withdrawn.

Claims 1,4-7 and 12-13 were also rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and further in view of Lerner et al.

The Glassman and the Paradissis patents have been discussed above and detailed reasons have been given as to why these references fail to make the subject matter of claim 1 obvious. The Lerner patent has not cited Glassman or Paradissis and nothing in the Lerner patent would lead a skilled artisan to select teachings from Glassman or Paradissis. The Lerner patent describes a gastrointestinal drug delivery system for delivery of enterally administered compositions to specific locations along the GI tract. The invention is directed to a composition comprising a core and coating wherein the core contains drug with carrier material, which preferably swells in contact with GI fluid. The Lerner patent teaches a formulation which allows the slow introduction of fluid into the device, which swells the particulate matter and the particles eventually form channels

from the outer part of the device to the drug containing core so that the drug is than released through the channels. Lerner is limited to a teaching that the release the drug in particular site of action or absorption is to be controlled based on the various parameters such as thickness of the outer coating (essentially contains rate controlling agents), the amount of particulate embedded in the coating, the type of particulate embedded in the coating, the particle size distribution of the particulate embedded in the coating and the core carrier. This reference does not suggest the concept of combining a low dose drug with a highly soluble drug of micro matrix particles for controlled release.

For these reasons, it is requested that this ground of rejection be withdrawn.

Claims 1-2 were also rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and in view of Webb et al.(Webb).

Reconsideration is requested.

The Glassman and the Paradissis patents have been discussed above and detailed reasons have been given as to why these references fail to make the subject matter of claim 1 obvious. The Webb patent is not cited by Glassman or Paradissis and nothing in the Webb patent would lead a skilled artisan to select teachings from Glassman or Paradissis. Webb is limited to a disclosure of a compressed tablet, made by multiple compressions, which has discrete zones and is made from a formulation of an active drug having a sustained release profile. Cellulose ethers in combination with surfactants and calcium carbonate are used to provide the sustained release properties of the dosage form. Nothing in Webb suggests the combination of a low dose drug with a highly soluble drug in a

controlled release formulation. For these reasons, it is requested that this ground of rejection be withdrawn.

Claims 33 and 34 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis, Timmins et al. (Timmins)and Webb.

Reconsideration is requested.

The Glassman, the Paradissis and the Webb patents have been discussed above and since they fail to disclose the combination of a low dose drug and a highly soluble drug they cannot disclose a low dose antidiabetic drug and a highly soluble anti-diabetic drug as claimed in claim 33.

The Timmins patent discloses a biphasic controlled release system for highly soluble drugs such as metformin alone or in combination, The dosage form has an inner and an outer phase and this patent teaches that the highly soluble drugs having a higher dosage strength and a narrow absorption window, will not give controlled release results in matrix or multiparticulate controlled release systems. In general, Timmins teaches that it is necessary to have extended residence times in the upper GI tract for metformin. The particular dosage forms are gastroretentive which by virtue of size and properties do no readily pass through the stomach. In any event, since the combined teachings of Timmins with the other references do not make obvious the combination of a low dose drug and a highly soluble drug, these combined teachings cannot disclose a low dose antidiabetic drug and a highly soluble anti-diabetic drug. For these reasons, it is requested that this ground of rejection be withdrawn.

Claims 33, 36 and 37 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and Timmins.

Claims 33, 40-43 and 48-50 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and Timmins.

Claims 33, 51-52 and 57 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and Timmins.

Claims 33, 58 and 59 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and Timmins.

Claims 33, 55-57 and 60 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and Timmins.

Claims 33 and 62 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and Timmins.

Claims 33 and 63-65 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and Timmins.

Claims 33 and 44-47 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and Timmins.

Claims 33 and 53-54 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and Timmins.

Claims 33 and 66 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and Timmins.

Claims 33 and 53-54 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and Timmins.

Claims 33 and 67 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and Timmins.

Claims 33 and 68-69 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and Timmins.

Claims 33 and 71-72 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis and Timmins.

Reconsideration is requested.

The Glassman and the Paradissis patents have been discussed above and since they fail to disclose the combination of a low dose drug and a highly soluble drug they cannot disclose a low dose antidiabetic drug and a highly soluble anti-diabetic drug as pointed out in claim 33.

As stated above, Timmins discloses a biphasic controlled release system for highly soluble drugs such as metformin alone or in combination, The dosage form has an inner and an outer phase and this patent teaches that the highly soluble drugs having a higher dosage strength and a narrow absorption window, will not give controlled release results in matrix or multiparticulate controlled release systems. In general, Timmins teaches that it is necessary to have extended residence times in the upper GI tract for metformin. The particular dosage forms are gastroretentive which by virtue of size and properties which prevent the dosage form from readily passing through the stomach. In any event, the combined teachings of Timmins with the other references do not make obvious the combination of a low dose drug and a highly soluble drug they cannot disclose a low dose antidiabetic drug and a highly soluble anti-diabetic drug according to claim 33. For

these reasons, it is requested that this ground of rejection be withdrawn.

Claims 33, 36-39 and 44-45 were rejected under 35 U.S.C.§103(a) as being unpatentable over Glassman in view of Paradissis, Timmins and Lerner.

Reconsideration is requested.

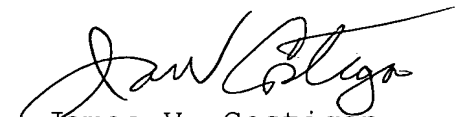
The Glassman and the Paradissis patents have been discussed above and since they fail to disclose the combination of a low dose drug and a highly soluble drug they cannot disclose a low dose antidiabetic drug and a highly soluble anti-diabetic drug as pointed out in claim 33.

The Lerner patent describes a gastrointestinal drug delivery system for delivery of enterally administered compositions to specific locations along the GI tract. The Timmins dosage form comprises a core and a coating wherein the core contains drug and carrier material which preferably swells in contact with GI fluid. The thickness of the outer coating and the embedded particulates control the release of the drug from the Lerner dosage form. This reference does not suggest the concept of combining a low dose antidiabetic drug with a highly soluble antidiabetic drug. For these reason, it is requested that this ground of rejection be withdrawn.

Claims 1-29 and 32-72 were also rejected for double patenting over Application Serial No. 10/522,989. This rejection has been rendered moot by the abandonment of Serial No. 10/522,989.

An early and favorable action is earnestly solicited.

Respectfully submitted,



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